

What is claimed is:

1. An isolated mammalian cell-surface estrogen receptor characterized by
  - 5 (a) a non-stereospecific binding affinity for  $17\alpha$ -estradiol and  $17\beta$ -estradiol;
  - (b) at least one epitope in common with the ligand-binding domain of ER- $\alpha$ ; and
  - 10 (c) increased presence at caveolar or caveolar-like microdomains of cells on which the receptor is present.
2. The receptor of claim 1, wherein the receptor is a human receptor.
- 15 3. A composition of matter comprising a lipid membrane, other than that of an intact cell, comprising the receptor of claim 1 operably situated therein.
- 20 4. The composition of claim 3, wherein the receptor is a human receptor.
5. A method for determining whether an agent specifically binds to the receptor of claim 1 which comprises
  - 25 (a) contacting the receptor with the agent under suitable conditions;
  - (b) detecting the presence of any complex formed between the receptor and the agent; and
  - 30 (c) determining whether the complex detected in step (b) is the result of specific binding between the agent and receptor, thereby determining whether the agent specifically binds to the receptor.

6. The method of claim 5, wherein the receptor is a human receptor.
7. The method of claim 5, wherein the receptor is operably  
5 situated within a lipid membrane.
8. A method for determining the affinity with which an agent binds to the receptor of claim 1 relative to that with which a known ligand binds the receptor, which comprises  
10 (a) concurrently contacting the receptor with both the agent and a ligand that binds the receptor with a known affinity under conditions which permit the formation of a complex between the receptor and the ligand;  
15 (b) determining the amount of complex formed between the agent and the receptor; and  
(c) comparing the amount of complex determined in step (b) with the amount of complex formed between the agent and the receptor in the absence of the ligand,  
20 wherein (i) a ratio of agent in the complex determined in step (c) to that determined in step (b) greater than 2 indicates that the agent binds to the receptor with less affinity than does the ligand, (ii) a ratio of less than 2 indicates that  
25 the agent binds to the receptor with greater affinity than does the ligand, and (iii) a ratio of 2 indicates that the agent and ligand bind to the receptor with the same affinity.
- 30 9. The method of claim 8, wherein the receptor is a human receptor.
10. A method for determining whether an agent is an agonist of the receptor of claim 1, which comprises

- 5 (a) contacting the receptor with the agent under conditions which permit (i) the formation of a complex between the receptor and a known agonist of the receptor, and (ii) the generation of a detectable signal upon formation of a complex between the receptor and the known agonist; and
- 10 (b) determining whether a detectable signal is generated in step (a), the generation of such signal indicating that the agent is an agonist of the receptor.
11. The method of claim 10, wherein the signal comprises an increase in ERK1/2 phosphorylation.
- 15 12. A method for determining whether an agent is an antagonist of the receptor of claim 1, which comprises
- 20 (a) contacting the receptor with the agent, in the presence of a known agonist, under conditions which permit (i) the formation of a complex between the receptor and the agonist, and (ii) the generation of a detectable signal upon formation of a complex between the receptor and the agonist; and
- 25 (b) comparing the signal, if any, generated in step (a) with the signal generated in the absence of the agent, the generation of a signal in the agent's absence greater than that generated in the agent's presence indicating that the agent is an antagonist.
- 30 13. The method of claim 12, wherein the signal comprises an increase in ERK1/2 phosphorylation.
- 35 14. A method for activating the MAP kinase pathway of a cell having on its surface the receptor of claim 1 comprising contacting the cell with a concentration of  $17\alpha$ -estradiol of at least 0.1pM and less than 100pM under conditions

permitting the 17 $\alpha$ -estradiol to bind to the receptor, thereby activating the MAP kinase pathway in the cell.

15. The method of claim 14, wherein the cell is a human cell.
- 5 16. The method of claim 14, wherein the cell is selected from the group consisting of a neuronal cell, a uterine cell, a stem cell, and a pulmonary cell.
- 10 17. A method for treating a subject afflicted with a neurodegenerative disorder, comprising administering to the subject an amount of 17 $\alpha$ -estradiol sufficient to raise the subject's plasma 17 $\alpha$ -estradiol concentration to at least 0.1pM and less than 100pM, thereby treating the
- 15 subject.
18. A method for delaying the onset of a neurodegenerative disorder in a subject, comprising administering to the subject an amount of 17 $\alpha$ -estradiol sufficient to raise
- 20 the subject's plasma 17 $\alpha$ -estradiol concentration to at least 0.1pM and less than 100pM, thereby delaying the onset of the neurodegenerative disorder in the subject.
19. The method of claim 17 or 18, wherein the
- 25 neurodegenerative disorder is a stroke.
20. The method of claim 17 or 18, wherein the neurodegenerative disorder is Alzheimer's disease.
- 30 21. The method of claim 17 or 18, wherein the neurodegenerative disorder is Parkinson's disease.
22. The method of claim 17 or 18, wherein the subject is human.

23. A method for treating a subject afflicted with a neurodevelopmental disorder, comprising administering to the subject an amount of  $17\alpha$ -estradiol sufficient to raise the subject's plasma  $17\alpha$ -estradiol concentration to at least 0.1pM and less than 100pM, thereby treating the subject.
24. The method of claim 23, wherein the neurodevelopmental disorder is schizophrenia.
25. The method of claim 23, wherein the neurodevelopmental is Turner's syndrome.
26. The method of claim 23, wherein the neurodevelopmental disorder is Down's syndrome.
27. The method of claim 23, wherein the subject is human.
28. A method for treating a subject afflicted with a sexually dimorphic childhood disorder of cognition, comprising administering to the subject an amount of  $17\alpha$ -estradiol sufficient to raise the subject's plasma  $17\alpha$ -estradiol concentration to at least 0.1pM and less than 100pM, thereby treating the subject.
29. The method of claim 28, wherein the sexually dimorphic childhood disorder of cognition is a learning disability.
30. The method of claim 28, wherein the sexually dimorphic childhood disorder of cognition is infantile autism.

31. The method of claim 28, wherein the sexually dimorphic childhood disorder of cognition is delayed speech acquisition.
- 5 32. The method of claim 28, wherein the sexually dimorphic childhood disorder of cognition is attention deficit disorder.
33. The method of claim 28, wherein the subject is human.
- 10 34. A method for treating a subject afflicted with a uterine disorder, comprising administering to the subject an amount of  $17\alpha$ -estradiol sufficient to raise the subject's plasma  $17\alpha$ -estradiol concentration to at least 0.1pM and
- 15 less than 100pM, thereby treating the uterine disorder in the subject.
35. The method of claim 34, wherein the uterine disorder is Turner's syndrome.
- 20 36. The method of claim 34, wherein the subject is human.
37. A method for treating a subject afflicted with a pulmonary disorder, comprising administering to the
- 25 subject an amount of  $17\alpha$ -estradiol sufficient to raise the subject's plasma  $17\alpha$ -estradiol concentration to at least 0.1pM and less than 100pM, thereby treating the subject.
- 30 38. The method of claim 37, wherein the pulmonary disorder is immature lung development in a preterm infant.
39. The method of claim 37, wherein the subject is human.

40. A composition comprising (a) a pharmaceutically acceptable carrier and (b) a dose of  $17\alpha$ -estradiol which, when administered to a subject, is sufficient to raise the subject's plasma  $17\alpha$ -estradiol concentration to at least 0.1pM and less than 100pM.
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41. An article of manufacture comprising (a) a packaging material having therein an amount of  $17\alpha$ -estradiol sufficient, upon administration to a subject, to raise the subject's plasma  $17\alpha$ -estradiol concentration to at least 0.1pM and less than 100pM, and (b) a label indicating a use of the  $17\alpha$ -estradiol for treating a disorder selected from the group consisting of a neurodegenerative disorder, a neurodevelopmental disorder, a sexually dimorphic childhood disorder of cognition, a uterine disorder, and a pulmonary disorder.
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